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Vital Sign Assessments – BP, Pulse, Respiratory Rate, SaO₂

		Day 6 at 30 min, prior and	
	Day 0 and 3 at 30 min,	1, 2, 4, 8, 12, 20, 23, 36,	Day 13 and at 0.25,
0, 1, 4, 8, 12,	prior and 1, 2, 4, 8, 12, 20,	47, 60, 71, 84, 95, 108,	0.50, 0.75, 1, 2, 4, 8,
24 h	23, 36, 47, and 60 h post-	119, 132, 143, 156, and	12, 24, 48, and 72 h
preapplication	application of BTDS 5 and	164 h postapplication of	postremoval of
of BTDS 5	BTDS 10	BTDS 20	BTDS 20

		BTDS 5	BTDS 10	BTDS 20	BTDS 20
		Applied	Applied	Applied	Removed
Elderly					
Hypertensive:	Screening	BTDS 5	BTDS 10	BTDS 20	Follow Up
Elderly Healthy:	Screening	BTDS 5	BTDS 10	BTDS 20	Follow Up
Young Healthy:	Screening	BTDS 5	BTDS 10	BTDS 20	Follow Up
		Day 0	Day 3	Day 6	Day 13
					Day 17

0, 23, and 47 h	0, 23, 47, 71, 95, 119, and	0.25, 0.50, 0.75, 1,
postapplication of BTDS 5	143 h postapplication of	2, 4, 8, 12, 24, 48,
and BTDS 10	BTDS 20	and 72 h post-
		removal of BTDS 20

Pharmacokinetic Sampling

FIGURE 1

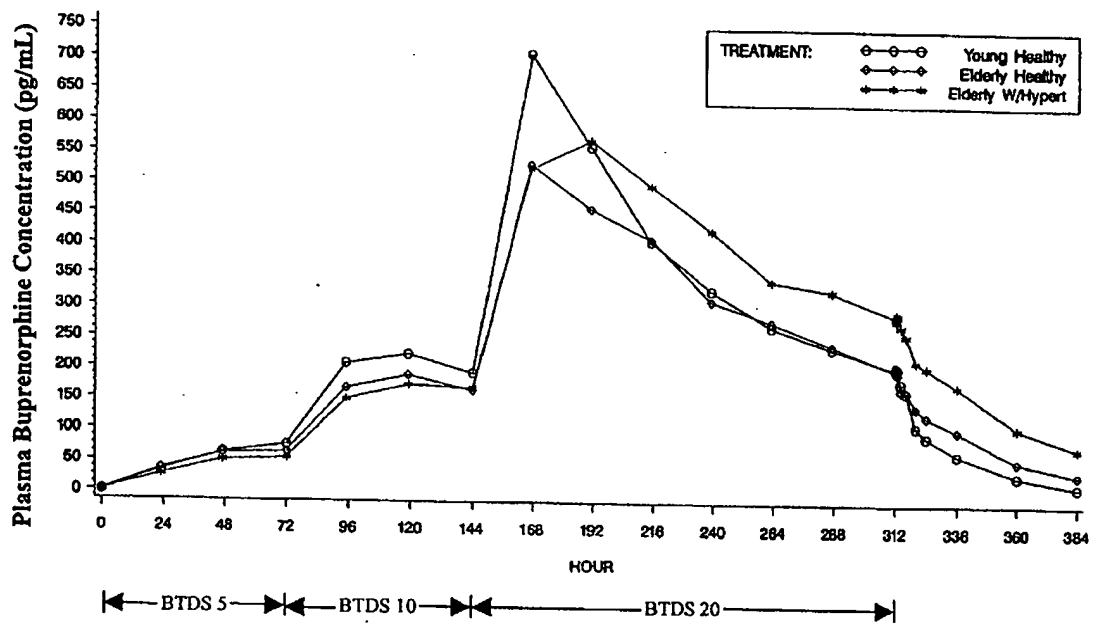


FIGURE 2

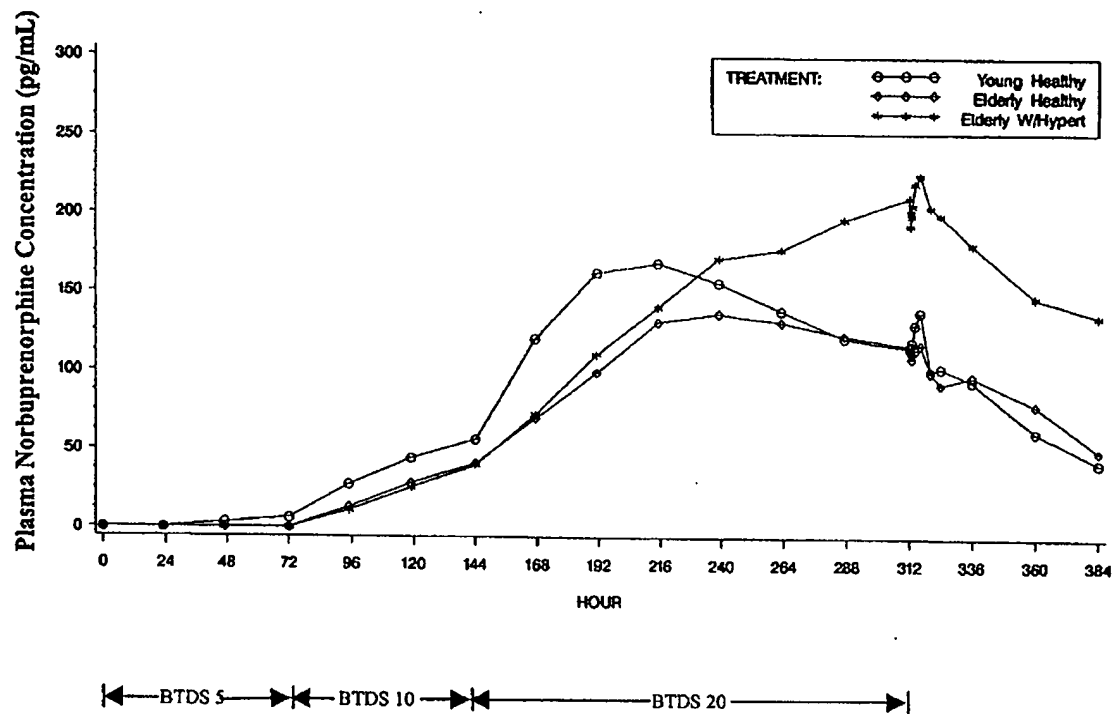


FIGURE 3

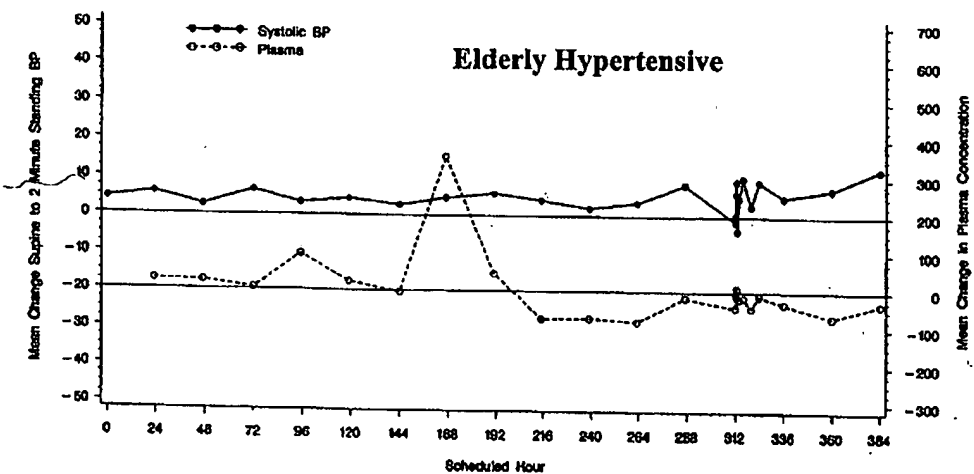
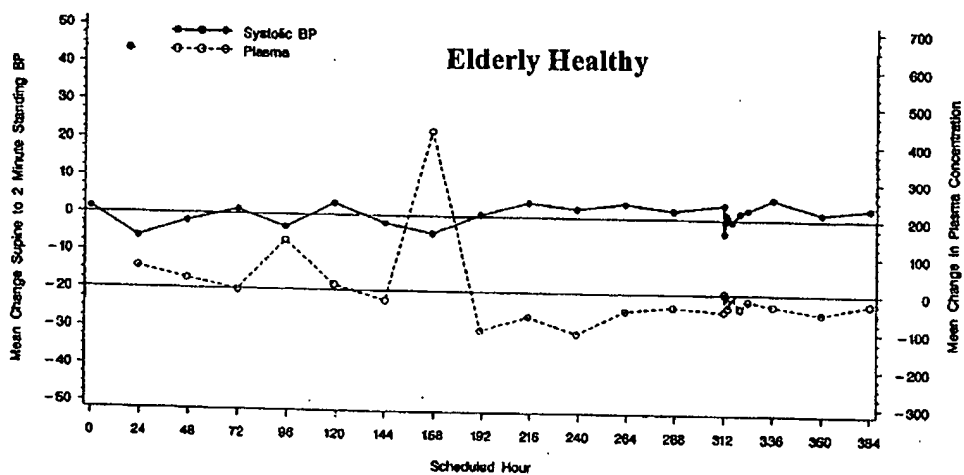
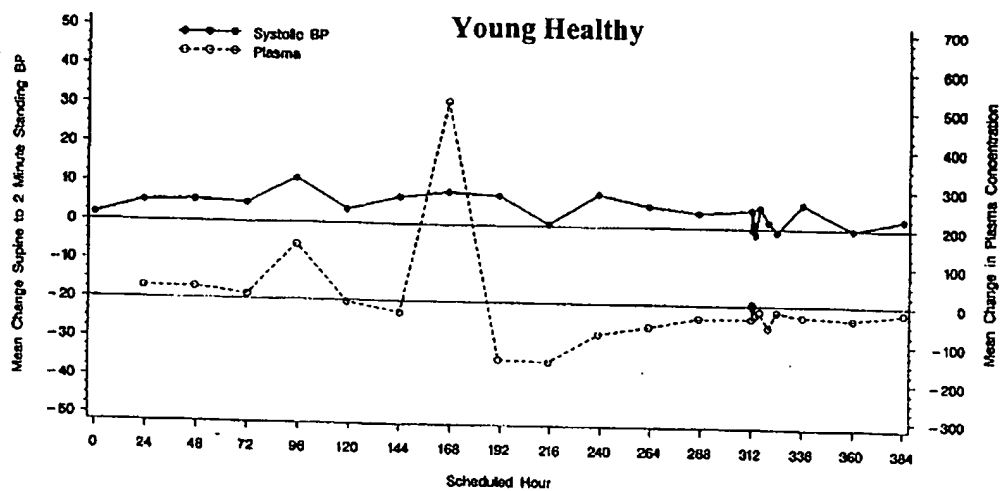


FIGURE 4

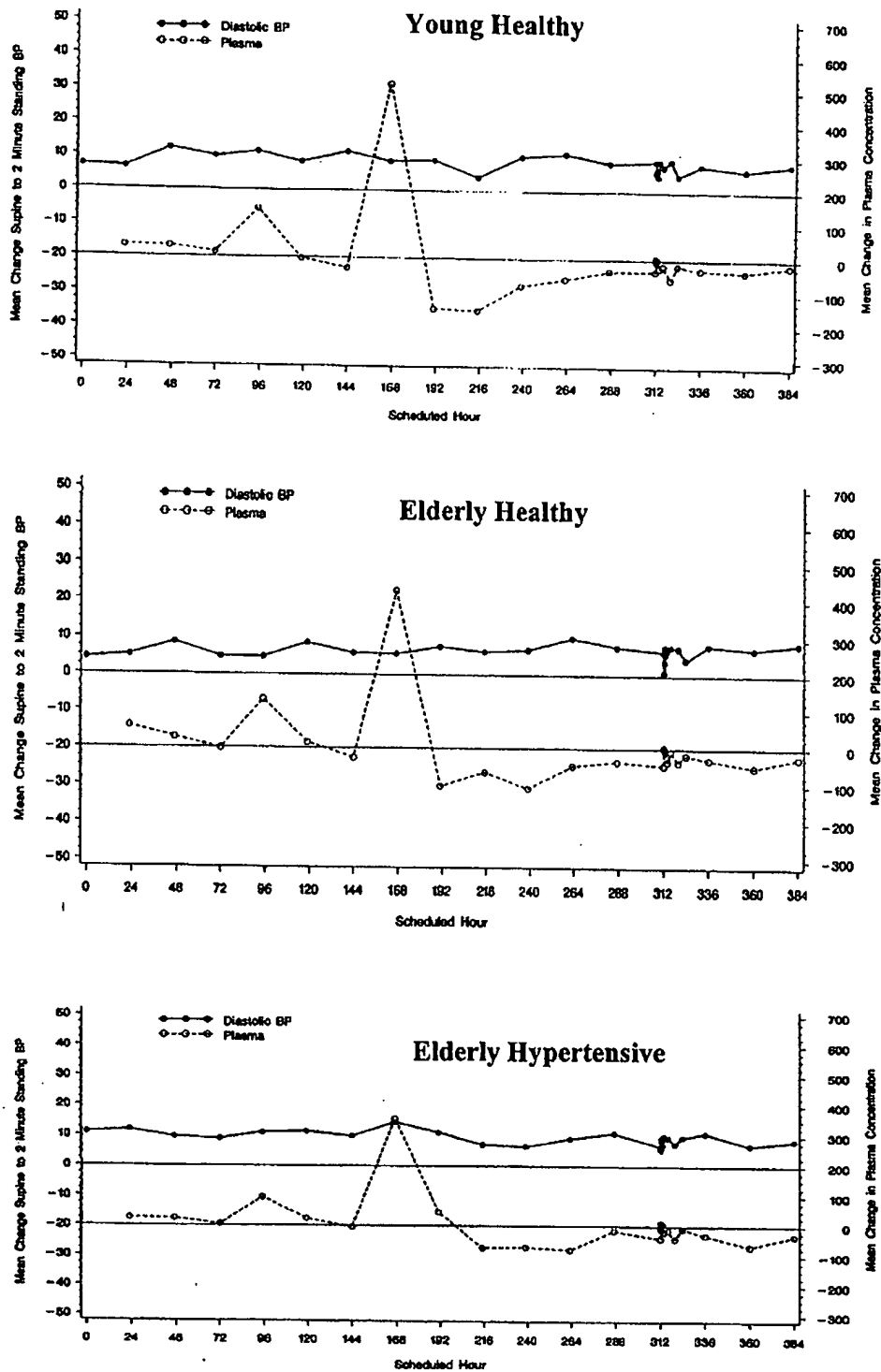


FIGURE 5

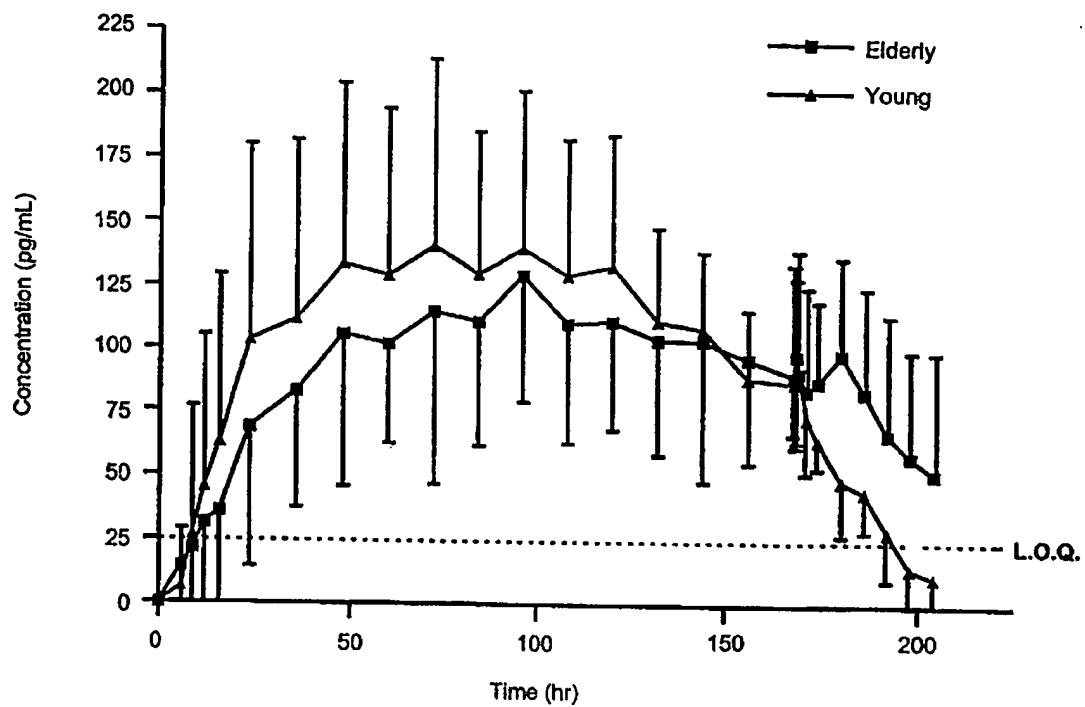


FIGURE 6

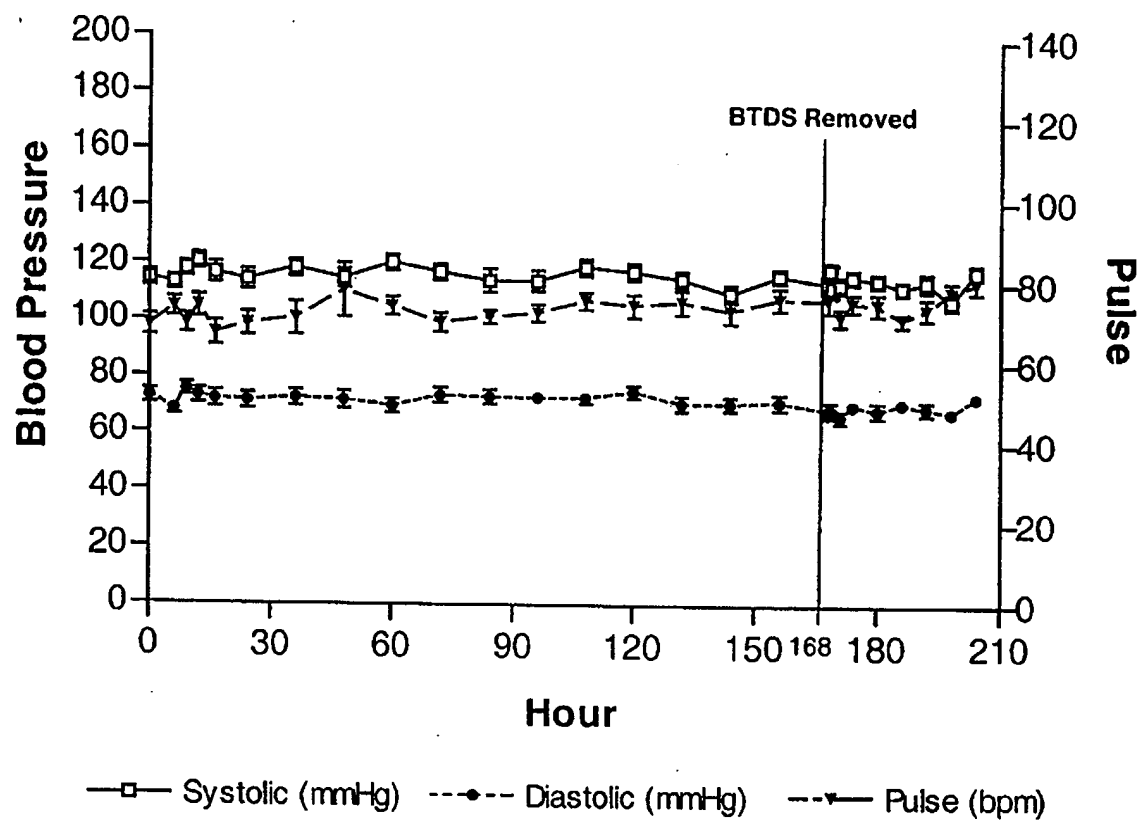


FIGURE 7

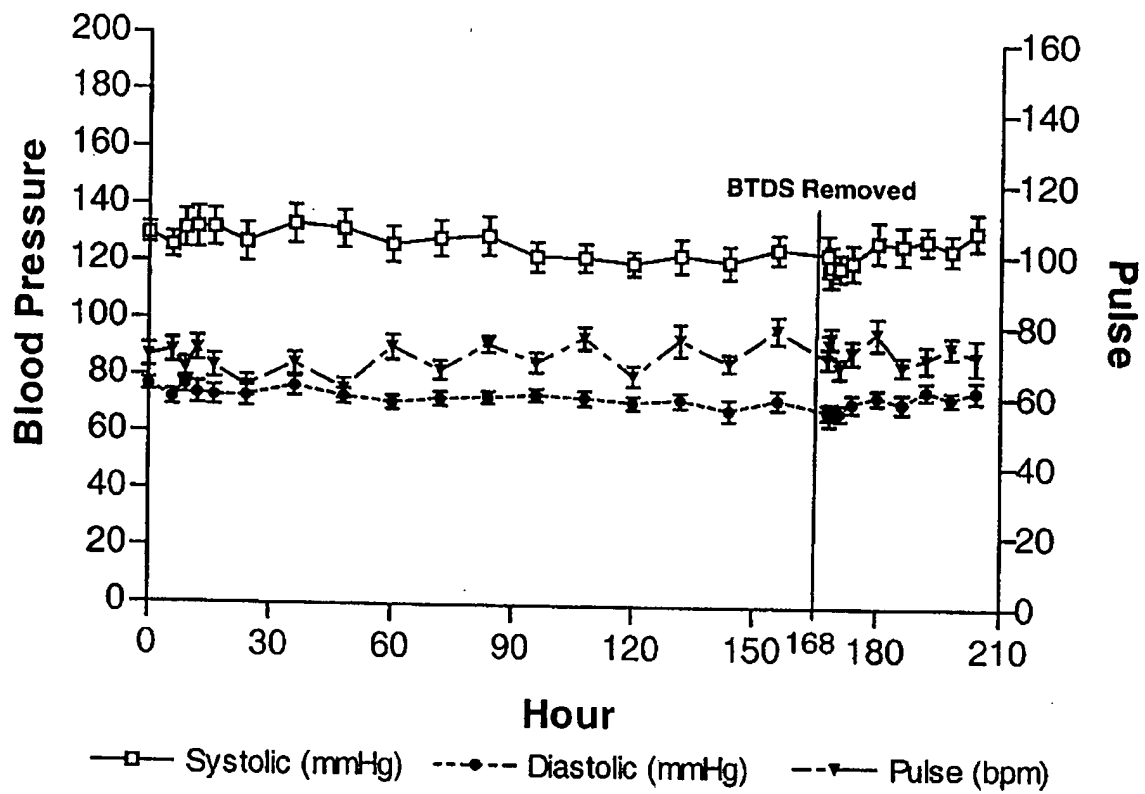
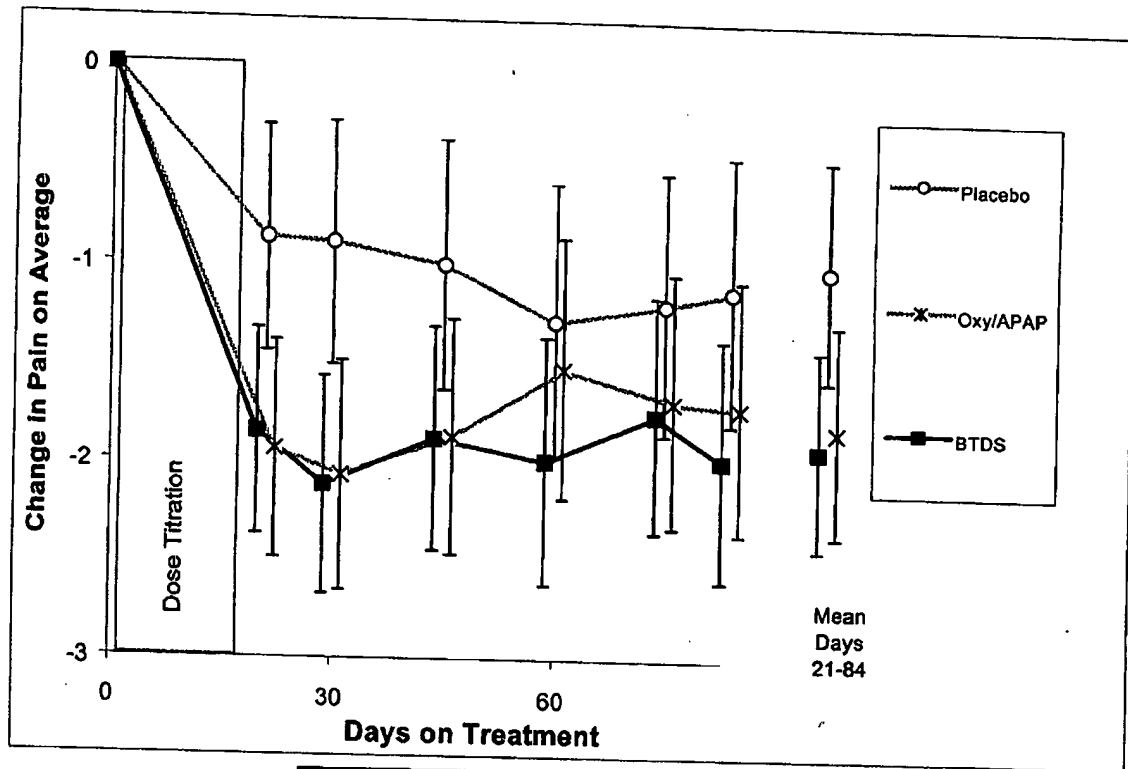


FIGURE 8



		Day 21	Day 30	Day 45	Day 60	Day 75	Day 84	RM 21-84
Placebo N=45	LS Mean \pm SEM	-0.87 \pm 0.38	-0.89 \pm 0.41	-1.00 \pm 0.42	-1.28 \pm 0.46	-1.19 \pm 0.44	-1.12 \pm 0.45	-1.01 \pm 0.37
	N with data	34	23	22	18	18	18	45
	Pairwise vs. Placebo	P=0.016	P=0.013	ns	ns	ns	ns	ns
Oxy/APAP N= 42	LS Mean \pm SEM	-1.94 \pm 0.37	-2.07 \pm 0.39	-1.87 \pm 0.40	-1.52 \pm 0.44	-1.68 \pm 0.43	-1.71 \pm 0.43	-1.82 \pm 0.36
	N with data	31	32	29	29	28	27	42
	Pairwise vs. Placebo	P=0.016	P=0.013	ns	ns	ns	ns	ns
BTDS N= 46	LS Mean \pm SEM	-1.85 \pm 0.35	-2.12 \pm 0.37	-1.88 \pm 0.38	-1.99 \pm 0.42	-1.75 \pm 0.40	-1.98 \pm 0.41	-1.92 \pm 0.34
	N with data	33	29	25	23	21	22	46
	Pairwise vs. Placebo	P=0.025	P=0.0093	ns	ns	ns	ns	P=0.035

Least squares (LS) means - corrected by SAS Proc Mixed for baseline pain, center and opioid experience

Bar indicates time of dose titration; all BTDS patients started with BTDS 5 and titrated dose on Day 7 and/or Day 14

N = Number of patients with data at that visit; N for LOCF = N for the treatment group and was consistent over time

Bars at each data point indicate \pm 1.5 SEM

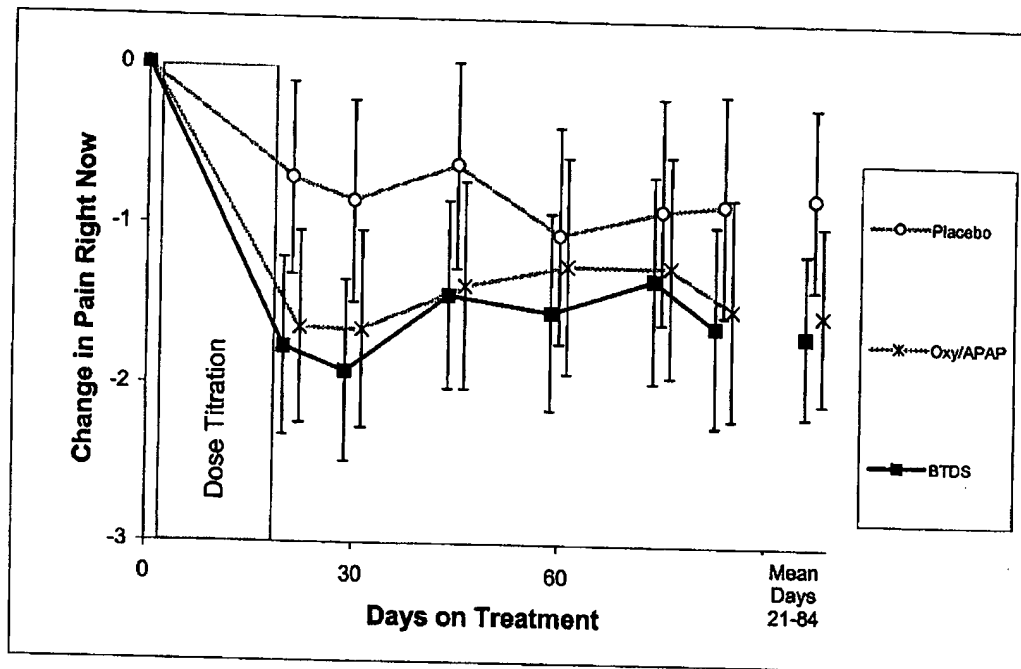
RM 21-84 values calculated via repeated measures analysis of all available data from Days 21-84 using SAS Proc Mixed

Pairwise vs. Placebo - results of comparison with placebo using SAS Proc Mixed

ns = difference not statistically significant ($P > 0.05$)

Bolding indicates statistically significant results

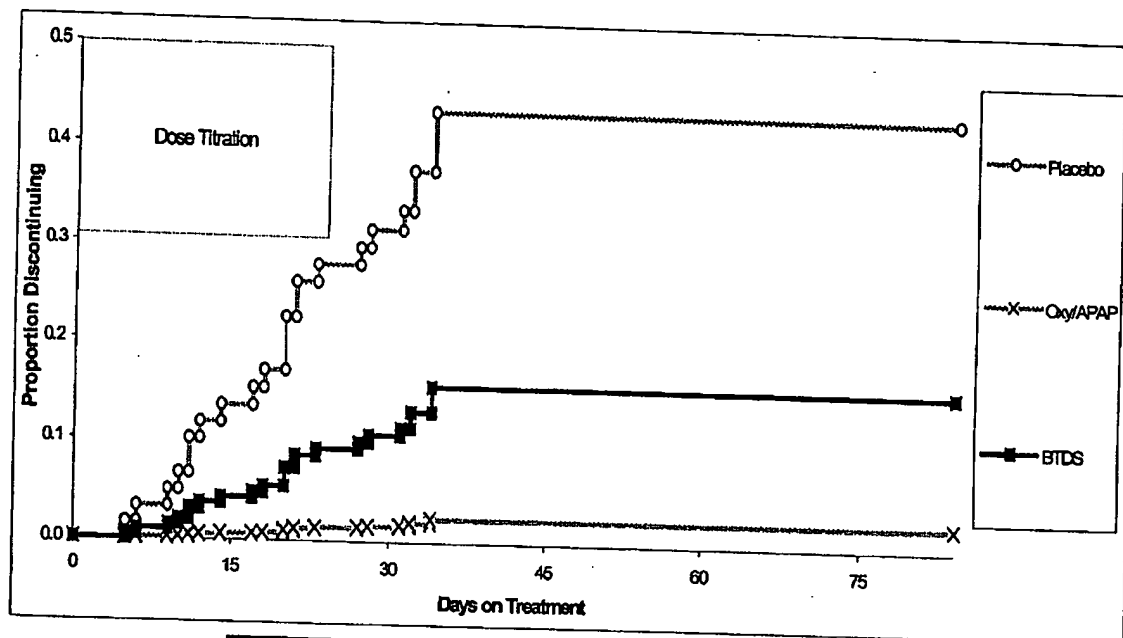
FIGURE 9



		Day 21	Day 30	Day 45	Day 60	Day 76	Day 84	RM 21-84
Placebo N=45	LS Mean \pm SEM	-0.71 \pm .040	-0.85 \pm 0.42	-0.82 \pm 0.43	-1.05 \pm 0.45	-0.89 \pm 0.47	-0.85 \pm 0.46	-0.80 \pm 0.38
	N with data	34	23	21	18	18	18	45
Oxy/APAP N= 42	LS Mean \pm SEM	-1.64 \pm 0.40	-1.65 \pm 0.41	-1.37 \pm 0.43	-1.24 \pm 0.45	-1.24 \pm 0.46	-1.50 \pm 0.46	-1.53 \pm 0.37
	N with data	31	32	29	29	28	27	42
	Pairwise vs. Placebo	P=0.049	ns	ns	ns	ns	ns	ns
BTDS N= 46	LS Mean \pm SEM	-1.76 \pm 0.37	-1.91 \pm 0.38	-1.43 \pm 0.39	-1.53 \pm 0.41	-1.32 \pm 0.43	-1.61 \pm 0.42	-1.66 \pm 0.34
	N with data	33	29	25	23	21	22	46
	Pairwise vs. Placebo	P=0.022	P=0.028	ns	ns	ns	ns	P=0.045

Least squares (LS) means - corrected by SAS Proc Mixed for age category, baseline pain, center and opioid experience
 Bar indicates time of dose titration: all BTDS patients started with BTDS 5 and titrated dose on Day 7 and/or Day 14
 N = Number of patients with data at that visit; N for LOCF = N for the treatment group and was consistent over time
 Bars at each data point indicate ± 1.5 SEM
 RM 21-84 values calculated via repeated measures analysis of all available data from Days 21-84 using SAS Proc Mixed
 Pairwise vs. Placebo - results of comparison with placebo using SAS Proc Mixed
 ns = difference not statistically significant ($P > 0.05$)
 Bolding indicates statistically significant results

FIGURE 10



	Day 0	Day 21	Day 30	Day 45	Day 60	Day 75	Day 84	Days 0-84	Pairwise vs Placebo
Placebo (N=45)									
Proportion discontinuing	0.000	0.260	0.315	0.435	0.435	0.435	0.435	-	
Number (at interval start)	45	29	26	22	19	19	18	-	
Drop out Lack of Efficacy	-	10	3	3	0	0	0	16	
Censored (total)	-	6	0	1	3	0	1	11	
Oxy/APAP (N=43)									
Proportion discontinuing	0.000	0.013	0.016	0.024	0.024	0.024	0.024	-	P=0.002
Number (at interval start)	43	32	32	29	29	28	27	-	
Drop out Lack of Efficacy	-	0	0	1	0	0	0	1	
Censored (total)	-	11	0	2	0	1	1	15	
BTDS (N=46)									
Proportion discontinuing	0.000	0.086	0.107	0.157	0.157	0.157	0.157	-	P=0.011
Number (at interval start)	46	32	29	25	23	22	22	-	
Drop out Lack of Efficacy	-	5	0	2	0	0	0	7	
Censored (total)	-	9	3	2	2	1	0	17	

Proportional hazards model using SAS proc PHREG with covariate correction for center and opioid experience
 Bar indicates time of dose titration: all BTDS patients started with BTDS 5 and titrated dose on Day 7 and/or Day 14
 ns = difference not statistically significant ($P > 0.05$)
 Bolding indicates statistically significant results

FIGURE 11